REMARKS

Claims 1-28 are withdrawn. Applicants have canceled claims 30 and 31. Applicants have amended claim 29 and have added new claims 32-56. The amended and new claims are supported throughout the specification as filed, e.g., at page 10, line 30 to page 11, line 13; page 22, line 29 to page 23, line 11; page 24, line 21 to page 25, line 7; page 34, lines 9-26; page 34, line 28 to page 35, line 18; page 35, line 20 to page 38, line 24; page 38, line 26 to page 40, line 4; and page 43, line 25 to page 44, line 15. No new matter has been added.

Upon entry of the current amendment, claims 1-29 and 32-56 will be pending and claims 29 and 32-56 will be under examination.

Rejections under 35 U.S.C. § 112, second paragraph

Claim 29 is rejected under 35 U.S.C. § 112, second paragraph, as "being incomplete for omitting essential steps, such omission amounting to a gap between the steps" (Office Action, page 2). Applicants have amended claim 29 by adding the steps of providing a follicular keratinocyte and treating the follicular keratinocyte, as suggested by the Examiner. The limitations of claim 30 have been incorporated into amended claim 29 and claim 30 has been canceled. Accordingly, the rejection should be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 29-31 are rejected under 35 U.S.C. § 112, first paragraph, "because the specification...does not reasonably provide enablement for the full scope encompassed by the claims" (Office Action, page 3). The Examiner argues generally that the claims are too broad in that they cover screening of any cell type. This rejection has been overcome by canceling claims 30 and 31 and substantially narrowing claim 29 (and the new claims) to recite a specific cell type: a follicular keratinocyte. The Examiner outlines the factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, as described by the court in In re Wands. Each of the factors is discussed below with regard to the present claims.

The nature of the invention

The invention is drawn to methods for identifying a compound that modulates hair growth and/or hair thickness by identifying a compound that modulates VEGF in a follicular keratinocyte.

The breadth of the claims

According to the Examiner, the pending claims are:

> very broad and encompass in vitro as well as in vivo methods. Furthermore, the broadly claimed method suggests that any compound which modulates the level or activity of VEGF in any cell-type would indicate that the compound is a modulator of hair growth or hair thickness (Office Action, page 4).

The breadth of the present claims is substantially narrowed. Claim 29, as amended, recites a method of selecting a compound that modulates hair growth or hair thickness by providing and treating a specific cell type, i.e., a follicular keratinocyte.

The unpredictability of the art and the state of the prior art

The Examiner cites Kozlowska et al. (Arch. Dermatol. Res. 290:661-668 (1998)) for the proposition that:

> one of skill in the art would recognize that VEGF expression in cells associated with hair follicles might be important for hair growth, but would not recognize VEGF expression in *other cells (i.e. cells not associated with hair follicles)* as important for hair growth (Office Action, page 5, emphasis added).

Claim 29, as amended, is limited to a follicular keratinocyte. While follicular cells in general might be recognized as important for hair growth, follicular keratinocytes in particular are not disclosed or suggested in the art to be involved in VEGF expression and hair growth.

Working Examples and Guidance in the Specification

The Examiner acknowledges only the example utilizing a mouse vibrissa organ culture system to assay the effect of VEGF on hair growth and hair thickness. However, the specification also provides significant additional data and examples to support the claims. For example, VEGF was shown to be expressed in follicular keratinocytes during hair growth (specification at page 18, lines 5-31). The specification also discloses a transgenic mouse model

in which VEGF overexpression in follicular keratinocytes led to accelerated hair regrowth and thickness compared to controls (specification at page 19, lines 7-28). Thus, the specification provides numerous experiments and ample guidance to support the claims.

Quantity of experimentation

The Examiner asserts that the claims are "very broad and encompass assaying of the test compound on VEGF expression/activity *in any cell-type*," necessitating further experimentation "to first establish the [sic] that VEGF expression/activity in *cells not associated with hair follicles* could be involved in hair growth" (Office Action, page 6, emphasis added). Claim 29, as amended, is limited to a follicular keratinocyte, a cell associated with hair follicles. Any experimentation needed to practice the presently claimed methods is routine. Art recognized techniques are available to assay VEGF. For example, Lachgar et al. (cited by the Examiner under 35 U.S.C. § 102) describe numerous assays to evaluate VEGF (albeit in a different cell type than recited the claims). These techniques include immunoassays (ELISA) to analyze VEGF protein levels and *in situ* hybridization to analyze VEGF mRNA levels.

Level of skill in the art

The Examiner notes that the level of skill in the art is deemed to be high.

The Examiner concludes that, based on the Wands factors, "the amount of experimentation required to perform the broadly claimed invention to the full scope encompassed by the claims is undue" (Office Action, page 6). Given the specific limitations of the present claims (narrowly directed to follicular keratinocytes), the high level of skill in the art, the extensive and detailed guidance provided by the specification, and the routine nature of the experimentation that may be required, the present claims are clearly enabled. Accordingly, Applicants request that the Examiner withdraw this rejection.

Rejections under 35 U.S.C. § 102

Claims 29-31 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lachgar et al. (British J. of Dermatol. 138:407-411 (1998)). According to the Examiner,

> Lachgar teaches a method of identifying compounds (such as minoxidil) that modulate hair growth by assaying the effect of the test compound on VEGF expression in cultured dermal papilla cells, *including keratinocytes* (Office Action, page 7, emphasis added).

This rejection has been met, in part, and is traversed, in part. The present claims recite a method of selecting a compound that modulates hair growth or hair thickness by assaying for VRGF in a follicular keratinocyte. Lachgar et al. disclose assaying the effect of minoxidil (a compound used for increasing growth) on VEGF expression in cultured dermal papilla cells. Lachgar et al. do not disclose assaying VEGF expression in keratinocytes, contrary to the Examiners statement. Dermal papilla cells and follicular keratinocytes are completely different and distinct cell types within the hair follicle. Dermal papilla cells are mesenchymal while keratinocytes are epidermal. Lachgar et al. say nothing about keratinocytes. Lachgar et al. teach that VEGF expression by dermal papilla cells regulates hair growth. Lachgar et al. do not teach or suggest that any other follicular cell type plays a role in VEGF expression and hair growth, much less in hair thickness. Accordingly, the present claims are not anticipated by Lachgar et al. and Applicants respectfully request that the Examiner withdraw this rejection.

Enclosed is a check for excess claim fees and a Petition for Extension of Time along with the required fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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